IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of	
Bradford C. Webb	
Serial No.: 08/240,941	
Filed: May 11, 1994	
For: Synthetic Viscoelastic Material for Ophthalmic Applications	

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner of Patents and Trademarks, Washington, D.C. 20231 on August 24, 1994

Declaration of Bradford C. Webb
Submitted Under 37 CFR 1.132

Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

Sir:

I, Bradford C. Webb declare that:

1. I am the inventor of the Synthetic Viscoelastic Material for Ophthalmic Applications claimed in the United States Patent Application 08/240,941 filed May 11, 1994. I am also the president of Vision Biology, Inc., assignee of record of the application.

2. I have read the claims of the subject patent application as well as the amended claim set forth in the amendment filed herewith. I am thoroughly familiar with the product claimed therein,

the product being manufactured by Vision Biology, Inc. under the name Cellugel™ materials, and the medical requirements of such a product.

3. I have personally prepared the Cellugel™ materials in accordance with the teachings of said application and the claims now pending and do represent and declare that the Cellugel™ materials supplied for the clinical trials reported herein are fully within the claims as originally filed, now pending, and as amended.

4. Cellugel™ materials are a high viscosity, high molecular weight cellulosic based viscoelastic material for use principally during ophthalmic surgery, particularly cataract surgery, to protect the delicate eye tissue and to maintain the volume of the eye.

5. Cellugel™ materials are not subject to many of the drawbacks of other cellulosic viscoelastic materials used for the same purposes.

6. An experimental HPMC material comprised of a 2% solution of Methocel E4M was incorrectly reported in the literature by Liesigagn. (Arshinoff later cited the article in his paper.) As a Cellugel VSF with a MW = 100,000 and a viscosity of 10,000 cps. With the exception of this erroneous reference, every other cellulosic viscoelastic material has a vicscosity of about 3,000 to 5,000 centipoise at 25°C. This is significantly less than the natural material found in the eye (the vitreous humor) or other viscoelastic

materials, particularly Healon®, used for this purpose. As a result, when one of these prior art cellulosic materials, including the prior low viscosity Cellugel VSF materials, are used to augment the eye's natural material during surgery, the volume in the eyeball is not properly maintained, thus interfering with surgical procedure and exposing the eye tissue to damage from surgical instruments. This represents a major drawback in the use of these materials.

7. I have read the three Arshinoff articles identified in the Information Disclosure Statement filed concurrently herewith. I am personally aware of the Cellugel VSF materials having a MWt = 100,000 and a V_oO = 10,000 reported therein as I prepared these materials and arranged for their experimental evaluation. That material, which is not the high viscosity, high molecular weight material claimed in the present application, is a partially treated E4M and had performance properties in line with other prior art HPMC materials and inferior to the claimed materials.

8. In the past, Healon® (hyaluronic acid) viscoelastic was the material of choice and it is the standard against which all other ophthalmic viscoelastic materials are judged. Healon® has a static viscosity of about 400,000cps and a reduced shear viscosity of about 80,000cps to 1,000cps at a shear rate of from 1 to 100 1/sec respectively. Cellugel™ materials, on the other hand, have a static viscosity of about 40,000 centipoise at 25°C with a shear viscosity of about 15,000 to about 3,000 at a shear rate of 1 to 100 ^{1}/sec.

9. Attached hereto as Attachment 1 is an enlarged reproduction of Figure 6 from Bothner et al. on which I have plotted the viscoelastic properties as determined experimental by me of a Cellugel™ material covered by the product's claims and prepared in accordance with the allowed process claims of the above referenced patent application. Cellugel™ has a shear viscosity over its full performance range more similar to Viscoat, a hyaluronic acid product, than prior art HPMC materials, and substantially similar to Healon® in the shear range of 1 to 1000 1/sec, which is more typical of the shear rates applied in ophthalmic phacoemulsification procedures.

10. Enclosed as Attachments 2 through 7 are tables presenting the statistical results determined in controlled clinical studies conducted in accordance with FDA guidelines. This data compares the clinical performance of the claimed materials with Healon®. These results show that the claimed material, in a clinical setting, is equivalent or superior to Healon® in all respects and, as such, far superior to any performance demonstrated by prior art HPMC materials.

11. These clinical trials demonstrate that the claimed invention does not suffer from the clinical problems shown in the literature to exist with prior art, low viscosity impure HPMC materials. In particular, no evidence of sterile hypopyons or fixed dilation pupils were observed.

12. Clinicians have reported to me, as part of their participation in the clinical trial, that the Cellugel™ material

performs as well as or better than Healon® in all instances and that this performance is superior to any HPMC material they have been used in the past.

DECLARATION

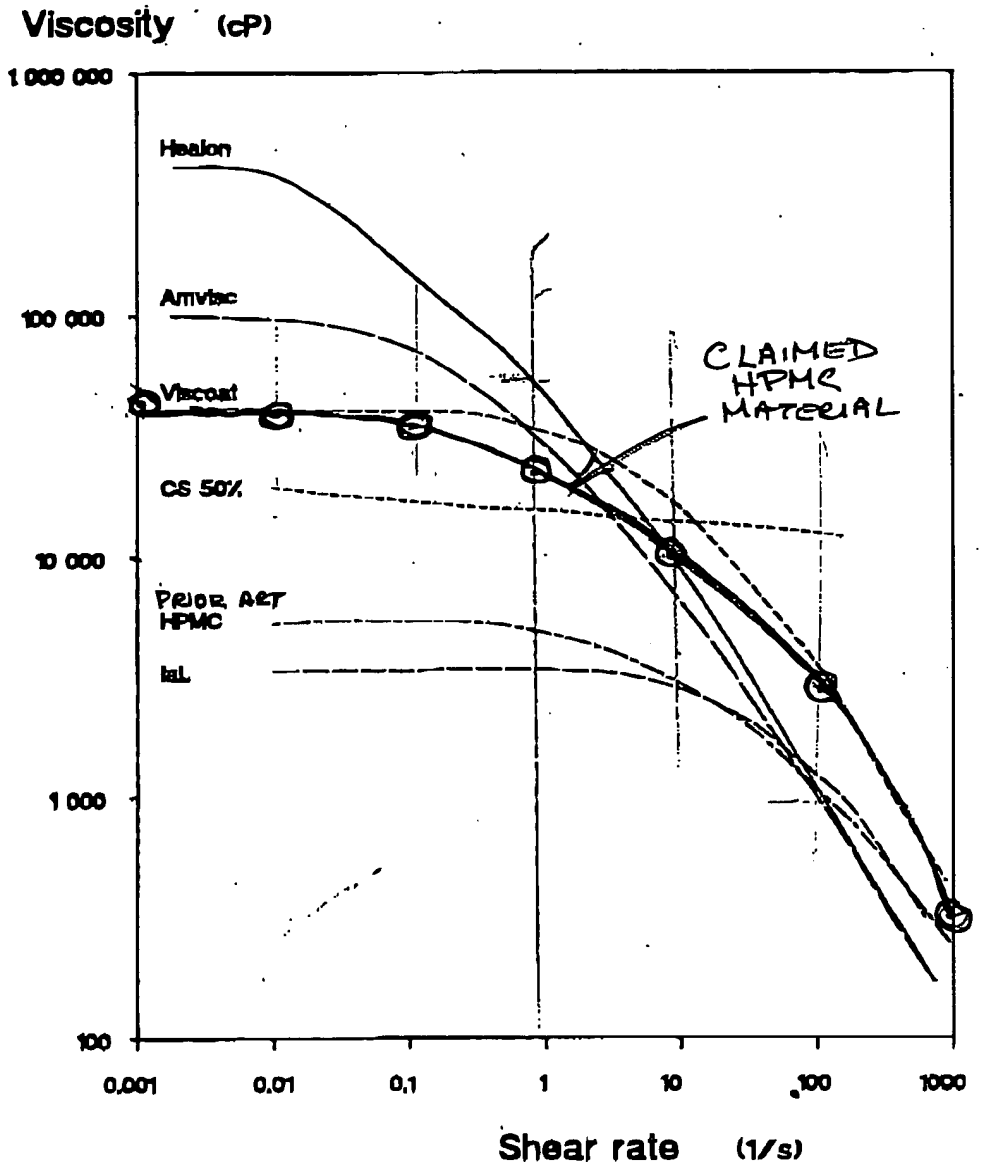
13. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that all statements were made with the knowledge that willful false statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both under 18 U.S.C. §1001 and that such willful false statements may jeopardize the validity of the application or any patent issuing thereupon.

Dated: July 31, 1994

Bradford C. Webb, Ph.D.
for U.S. Patent Application
No. 08/240,941

ATTACHMENT 1

Visc sity/Shear Rate Relationship*



* Bothner, et al. Figure 6 modified to include inv ntion.

ATTACHMENT 2

US Clinical Trial Results

- Total of 350 cases enrolled by April 1994
- Interim data analysis on 194 cases - 102 Cellugel, 92 Healon
- 59 Cases with 6 month followup
- PMA filing in late 1994
  - Marketing approval - late 1995

Trial Population Preop/Op Conditions

	Cellugel	Healon
- Cases	102	92
- Male	43%	36%
- Female	57%	64%
- Preop Glaucoma	16%	4%
- Diabetic Retinop.	2%	2%
- Mac. Degen.	7%	4%
- Phaco	85%	80%
- ECCE	15%	20%
- IOL Implanted	100%	100%

ATTACHMENT 3

Adverse Events Reported

- 20 Cases IOP Above 25 mm Hg at 24 hr.
- 11 Cellugel, 9 Healon
- All cases resolved immediately except 3 cases with IOP > 35 mm at 24 hr. visit
- Case 1 - Healon
  - » Complicated surgery
  - » IOP resolved to 14 mm by day 7
  - » Visual Acuity at 90 days postop 20/40 or better
- Case 2 - Cellugel
  - » Preoperative glaucoma
  - » Retained cortex, secondary surgical intervention

Adverse Events (contd.)

- Case 2 - contd.
  - » IOP 19 mm by 90 days postop
  - » Visual Acuity 20/40 or better
- Case 3 - Cellugel
  - » Complex extended surgery, PC rupture
  - » IOP 17 mm 90 days postop
  - » Visual Acuity 20/40 or better

■ Conclusion: there have been no adverse events that were related to the use of either viscoelastic in the trial

ATTACHMENT 4

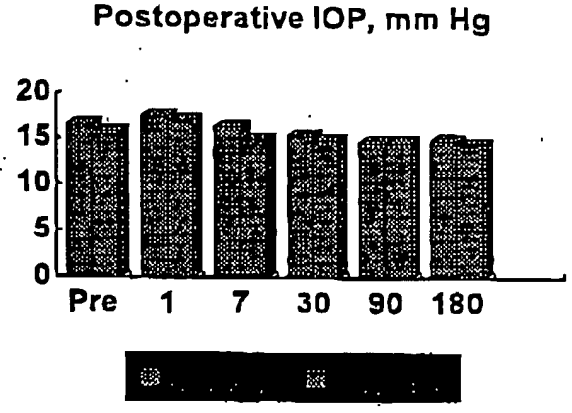
Postoperative IOP

- Postoperative IOP, mm Hg, +/- 1.5 mm (*)

Form	Cellugel	Healon
Preop	16.5	15.8
1	17.5	17.0
2	16.3	14.9
3	15.3	14.8
4	14.6	14.6
5	14.8	14.4

- (*) Exclusive of 3 cases with IOP > 35 mm

Postoperative IOP

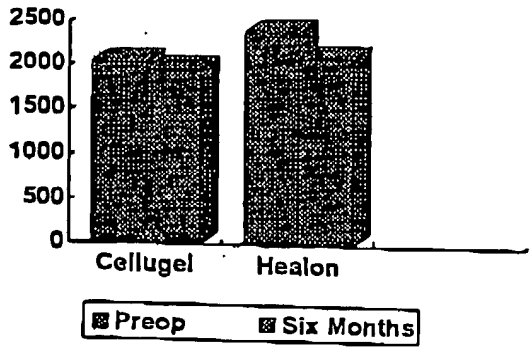


ATTACHMENT 5

Endothelial Cell Counts

	Cellugel	Healon
Cases	29	26
Preop	2,025 +/- 533	2,393 +/- 463
Form 5	1,952 +/- 476	2,098 +/- 457
	3.6% loss	12.3% loss

Endothelial Cell Counts



ATTACHMENT 6

Postoperative Visual Acuity 90 days postop

–	Cellugel	Healon
– Cases	69	65
– 20/40 or better	75.4%	70.8%
– 20/80	10.1%	15.4%
– 20/100	1.4%	1.5%
– 20/200 or worse	1.4%	1.5%
– No VA reported	11.6%	9.2%

Postop. Complications 90 days postop

–	Cellugel	Healon
– Cases	69	65
– Corneal Edema	0.0%	4.6%
– Iritis	1.4%	3.1%
– Hyphema	0.0%	0.0%
– Macular Edema	5.8%	3.1%
– Macular Degeneration	1.4%	7.7%
– Sec. Glaucoma	1.4%	0.0%
– PC Haze	11.6%	24.6%
– Cortical R mnants	0.0%	0.0%

TELEFAX

NO. 703/308-4556

FOR IMMEDIATE DELIVERY TO

EXAMINER Z. FAY

THANK YOU!

DATE: October 12, 2000

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In re: **Application No. 08/870,199**
Docket: 1560B

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